nucleic acid molecule consists of the nucleotide sequence shown in SEQ ID NO:1. In another preferred embodiment, the nucleic acid molecule includes a fragment of at least 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, or 900 nucleotides (e.g., contiguous nucleotides) of the nucleotide sequence of SEQ ID NO: 1, or a complement thereof.

In another embodiment, a SLIC-1 nucleic acid molecule includes a nucleotide sequence encoding a protein having an amino acid sequence sufficiently identical to the amino acid sequence of SEQ ID NO:2. In a preferred embodiment, a SLIC-1 nucleic acid molecule includes a nucleotide sequence encoding a protein having an amino acid sequence at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identical to the entire length of the amino acid sequence of SEQ ID NO:2.

In another preferred embodiment, an isolated nucleic acid molecule encodes the amino acid sequence of human SLIC-1. In yet another preferred embodiment, the nucleic acid molecule includes a nucleotide sequence encoding a protein having the amino acid sequence of SEQ ID NO:2. In yet another preferred embodiment, the nucleic acid molecule is at least 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, or 900 nucleotides in length. In a further preferred embodiment, the nucleic acid molecule is at least 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, or 900 nucleotides in length and encodes a protein having a SLIC-1 activity (as described herein).

Another embodiment of the invention features nucleic acid molecules, preferably SLIC-1 nucleic acid molecules, which specifically detect SLIC-1 nucleic acid molecules

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relative to nucleic acid molecules encoding non-SLIC-1 proteins. For example, in one embodiment, such a nucleic acid molecule is at least 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900 or more nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1, or a complement thereof.

In other preferred embodiments, the nucleic acid molecule encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1 under stringent conditions. --.

Replace the paragraph beginning on page 5, at line 1, with the following paragraph:

-- In a preferred embodiment, a SLIC-1 protein includes at least one immunoreceptor tyrosine-based activation motif and has an amino acid sequence at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identical to the amino acid sequence of SEQ ID NO:2. --.

Replace the paragraph beginning on page 5, at line 13, with the following paragraph:

-- In another embodiment, the invention features fragments of the protein having the amino acid sequence of SEQ ID NO:2, wherein the fragment comprises at least 15 amino acids (e.g., 15 contiguous amino acids) of the amino acid sequence of SEQ ID NO:2. In one embodiment, a SLIC-1 protein has amino acid residues 1-88 of SEQ ID NO:2. In another embodiment, a SLIC-1 protein has amino acid residues 1-60 of SEQ ID NO:2. In a further embodiment, a SLIC-1 protein has amino acid residues 1-226 of

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SEQ ID NO:2. In another embodiment, a SLIC-1 protein has the amino acid sequence of SEQ ID NO:2. --.

Replace the paragraph beginning on page 7, at line 9, with the following paragraph:

-- *Figures 1A and 1B* depict the cDNA sequence and predicted amino acid sequence of human SLIC-1. The nucleotide sequence corresponds to nucleic acids 1 to 951 of SEQ ID NO:1. The amino acid sequence corresponds to amino acids 1 to 316 of SEQ ID NO: 2. --.

On pages 11 and 12, replace the paragraph beginning on page 11, at line 33, with the following paragraph:

-- The nucleotide sequence of the isolated human SLIC-1 cDNA and the predicted amino acid sequence of the human SLIC-1 polypeptide are shown in Figures 1A and 1B and in SEQ ID NOs:1 and 2, respectively. --.

Replace the two paragraphs beginning on page 12, at line 35, and ending on page 13, at line 13, with the following two paragraphs:

-- A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, or a portion thereof, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or portion of the nucleic acid sequence of SEQ ID NO:1, as a hybridization probe, SLIC-1 nucleic acid molecules can be isolated using standard hybridization and cloning techniques (e.g., as described in Sambrook, J., Fritch, E. F., and Maniatis, T. Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989).

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Moreover, a nucleic acid molecule encompassing all or a portion of SEQ ID NO:1 can be isolated by the polymerase chain reaction (PCR) using synthetic oligonucleotide primers designed based upon the sequence of SEQ ID NO:1. --.

Replace the three paragraphs beginning on page 13, at line 24, and ending on page 14, at line 26, with the following three paragraphs:

-- In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1, or a portion of any of these nucleotide sequences. A nucleic acid molecule which is complementary to the nucleotide sequence shown in SEQ ID NO:1, is one which is sufficiently complementary to the nucleotide sequence shown in SEQ ID NO:1, such that it can hybridize to the nucleotide sequence shown in SEQ ID NO:1, thereby forming a stable duplex.

In still another preferred embodiment, an isolated nucleic acid molecule of the present invention comprises a nucleotide sequence which is at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identical to the entire length of the nucleotide sequence shown in SEQ ID NO:1, or a portion of any of these nucleotide sequences.

Moreover, the nucleic acid molecule of the invention can comprise only a portion of the nucleic acid sequence of SEQ ID NO:1, for example, a fragment which can be used as a probe or primer or a fragment encoding a portion of a SLIC-1 protein, e.g., a biologically active portion of a SLIC-1 protein. The nucleotide sequence determined from the cloning of the SLIC-1 gene allows for the generation of probes and primers designed for use in identifying and/or cloning other SLIC-1 family members, as well as

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SLIC-1 homologues from other species. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12 or 15, preferably about 20 or 25, more preferably about 30, 35, 40, 45, 50, 55, 60, 65, 75, 80, 85, 90, 95, 100, 150, or 200 or more consecutive nucleotides of a sense sequence of SEQ ID NO: 1, of an anti-sense sequence of SEQ ID NO:1, or of a naturally occurring allelic variant or mutant of SEQ ID NO: 1. In one embodiment, a nucleic acid molecule of the present invention comprises a nucleotide sequence which is greater than 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900 or more nucleotides in length and hybridizes under stringent hybridization conditions to a nucleic acid molecule of SEQ ID NO:1. --.

Replace the three paragraphs beginning on page 14, at line 35, and ending on page 15, at line 21, with the following three paragraphs:

-- A nucleic acid fragment encoding a "biologically active portion of a SLIC-1 protein" can be prepared by isolating a portion of the nucleotide sequence of SEQ ID NO:1, which encodes a polypeptide having a SLIC-1 biological activity (the biological activities of the SLIC-1 proteins are described herein), expressing the encoded portion of the SLIC-1 protein (e.g., by recombinant expression in vitro) and assessing the activity of the encoded portion of the SLIC-1 protein.

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence shown in SEQ ID NO:1, due to degeneracy of the genetic code and thus encode the same SLIC-1 proteins as those encoded by the nucleotide sequence shown in SEQ ID NO:1. In another embodiment, an isolated nucleic acid

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molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NO:2.

In addition to the SLIC-1 nucleotide sequences shown in SEQ ID NO:1, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of the SLIC-1 proteins may exist within a population (e.g., the human population). Such genetic polymorphism in the SLIC-1 genes may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules which include an open reading frame encoding a SLIC-1 protein, preferably a mammalian SLIC-1 protein, and can further include non-coding regulatory sequences, and introns. --.

Replace the paragraph beginning on page 16, at line 3, with the following paragraph:

-- Moreover, nucleic acid molecules encoding other SLIC-1 family members and, thus, which have a nucleotide sequence which differs from the SLIC-1 sequences of SEQ ID NO: 1. For example, another SLIC-1 cDNA can be identified based on the nucleotide sequence of human SLIC-1. Moreover, nucleic acid molecules encoding SLIC-1 proteins from different species, and which, thus, have a nucleotide sequence which differs from the SLIC-1 sequences of SEQ ID NO: 1. For example, a mouse SLIC-1 cDNA can be identified based on the nucleotide sequence of a human SLIC-1. --.

Replace the paragraph beginning on page 16, at line 21, with the following paragraph:

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-- Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 15, 20, 25, 30 or more nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1. In other embodiment, the nucleic acid is at least 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900 or more nucleotides in length. --.

Replace the bridging paragraph beginning on page 17, at line 35, with the following paragraph:

-- In addition to naturally-occurring allelic variants of the SLIC-1 sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NO:1, thereby leading to changes in the amino acid sequence of the encoded SLIC-1 proteins, without altering the functional ability of the SLIC-1 proteins. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NO:1. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of SLIC-1 (e.g., the sequence of SEQ ID NO:2) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are conserved among the SLIC-1 proteins of the present invention, e.g., those present in a immunoreceptor tyrosine-based activation motif, are predicted to be particularly unamenable to alteration. Furthermore, additional amino acid residues that are conserved between the SLIC-1 proteins of the present invention and other members of the SLIC family are not likely to be amenable to alteration. --.

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Replace the paragraph beginning on page 18, at line 21, with the following paragraph:

-- An isolated nucleic acid molecule encoding a SLIC-1 protein identical to the protein of SEQ ID NO:2, can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced into SEQ ID NO:1 by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in a SLIC-1 protein is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of a SLIC-1 coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for SLIC-1 biological activity to identify mutants

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that retain activity. Following mutagenesis of SEQ ID NO:1, the encoded protein can be expressed recombinantly and the activity of the protein can be determined. --.

Replace the paragraph beginning on page 21, at line 8, with the following paragraph:

-- In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead ribozymes (described in Haselhoff and Gerlach (1988) Nature 334:585-591)) can be used to catalytically cleave SLIC-1 mRNA transcripts to thereby inhibit translation of SLIC-1 mRNA. A ribozyme having specificity for a SLIC-1-encoding nucleic acid can be designed based upon the nucleotide sequence of a SLIC-1 cDNA disclosed herein (i.e., SEQ ID NO:1). For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a SLIC-1-encoding mRNA. See, e.g., Cech et al. U.S. Pat. No. 4,987,071; and Cech et al. U.S. Pat. No. 5,116,742. Alternatively, SLIC-1 mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel, D. and Szostak, J. W. (1993) Science 261:1411-1418. --.

Replace the paragraph beginning on page 37, at line 36, with the following paragraph:

-- A transgenic animal of the invention can be created by introducing a SLIC-1-encoding nucleic acid into the male pronuclei of a fertilized oocyte, e.g., by

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microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The SLIC-1 cDNA sequence of SEQ ID NO:1 can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of a human SLIC-1 gene, such as a mouse or rat SLIC-1 gene, can be used as a transgene. Alternatively, a SLIC-1 gene homologue, such as another SLIC-1 family member, can be isolated based on hybridization to the SLIC-1 cDNA sequences of SEQ ID NO:1 and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to a SLIC-1 transgene to direct expression of a SLIC-1 protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Pat. Nos. 4,736,866 and 4,870,009, both by Leder et al., U.S. Pat. No. 4,873,191 by Wagner et al. and in Hogan, B., Manipulating the Mouse Embryo, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of a SLIC-1 transgene in its genome and/or expression of SLIC-1 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding a SLIC-1 protein can further be bred to other transgenic animals carrying other transgenes. --.

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Replace the paragraph beginning on page 57, at line 14, with the following paragraph:

-- An exemplary method for detecting the presence or absence of SLIC-1 protein or nucleic acid in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting SLIC-1 protein or nucleic acid (e.g., mRNA, or genomic DNA) that encodes SLIC-1 protein such that the presence of SLIC-1 protein or nucleic acid is detected in the biological sample. A preferred agent for detecting SLIC-1 mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to SLIC-1 mRNA or genomic DNA. The nucleic acid probe can be, for example, the SLIC-1 nucleic acid set forth in SEQ ID NO:1, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to SLIC-1 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein. --.

Replace the paragraph beginning on page 72, at line 15, with the following paragraph:

-- Accordingly, the invention is based, at least in part, on the discovery of a human gene encoding a novel protein, referred to herein as SLIC-1. The nucleotide sequence encoding the human SLIC-1 protein is shown in Figures 1A and 1B and is set forth as SEQ ID NO:1. The protein encoded by this nucleic acid comprises about 316 amino acids and has the amino acid sequence shown in Figures 1A and 1B and set forth as SEQ ID NO:2. --.

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Replace the paragraph beginning on page 73, at line 11, with the following paragraph:

-- The nitrocellulose membranes were blocked at 4°C overnight in 3% BSA (SIGMA) in Tris Buffered Saline (TBS) with 0.1% Tween-20. The membranes were washed for 7 minutes in TBS-0.1% Tween, and then incubated for 1 hour in a 1:2500 dilution of affinity-purified rabbit anti-SLIC-1 polyclonal antibodies (Research Genetics, Inc.). These antibodies were generated by immunizing rabbits with a polypeptide antigen having the amino acid sequence QERLEESQLRRPTPR (SEQ ID NO:5) conjugated to KLH. The membranes were washed three times in TBS-0.1% Tween, incubated for 1 hour with a secondary antibody to detect rabbit immunoglobulin, and developed using the ECL Western Blotting Detection System (Amersham). Mock transfections and Western blot analysis using unrelated purified polyclonal rabbit IgG (Serotec) were performed in parallel as controls. The results of this analysis are shown in Figure 2. The SLIC-1 protein exhibits an apparent molecular weight of approximately 45 kD by SDS-PAGE analysis. --.

Replace the paragraph beginning on page 73, at line 27, with the following paragraph:

-- A DNA construct that allows the expression of full length SLIC-1 as a fusion protein with a T7 protein tag was generated as follows. A mutated primer for the 5' sequence of SLIC-1 was designed to introduce a T7 tag directly upstream of the initiation codon of SLIC-1 in vector pED.Uran-5 by PCR. The T7 tag encodes the amino acid sequence MASMTGGQQMG (SEQ ID NO:6). The PCR reaction generated a product of approximately 380 bp, spanning the N-terminal end of SLIC-1 beyond an

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Ascl restriction site. A 5' SaiII site and this Ascl site were used to replace the original N-terminal end of SLIC-1 in pED.Uran-5 with the PCR product containing the T7 tag. The resulting vector was designated pED.T7Uran-5 and encodes all 316 amino acids of SLIC-1. The pED.T7Uran-5 vector was further used to create three truncated forms of SLIC-1 as follows. The vector pED.T7U5AA226 encodes for the first 226 amino acids of SLIC-1, and was generated by restriction digestion of pED.T7Uran-5 with NotI and Ascl and ligation of the plasmid with a NotI/XbaI linker that also comprises a Stop codon to terminate transcription. A similar approach was used to create pED.T7U5AA160, a 160 amino acid short form of SLIC-1 that was generated by restriction digestion of pED.T7Uran-5 with Ascl and XbaI and ligation with an appropriate linker. The vector PED.T7U5AA88 was generated by PCR using the original 5' primer for pED.T7Uran-5 and a newly designed 3' primer which introduced a Stop codon and an additional XbaI site after amino acid residue 88 in SLIC-1. The XbaI and SalI sites in pED.T7Uran-5 were then used to replace the sequence for full length SLIC-1 with this truncated form. --.

IN THE SEQUENCE LISTING:

Replace the prior Sequence Listing with the Sequence Listing submitted herewith.

IN THE CLAIMS:

26. (Twice Amended) A method for identifying a compound which inhibits the binding of a SLIC-1 protein to PSGL-1, comprising:

i) contacting said SLIC-1 protein with a test compound; and

ii) determining the effect of the test compound on the binding of said SLIC-1 protein to PSGL-1;

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